

# EXHIBIT F

**Supplemental Report of Alexander P. Ruggieri, MD, MHS**

I hold a Doctor of Medicine degree from Georgetown University and a Master's Degree in Health Science from Johns Hopkins University of School of Public Health. I practiced internal medicine and rheumatology subsequent to my medical training. I left the practice of medicine to pursue a National Library of Medicine Fellowship in Medical Informatics at the University of Minnesota and the Mayo Clinic College of Medicine. This fellowship included didactic training in computer science, epidemiology and biostatistics. After completing my fellowship, I worked in academic medicine and in the pharmaceutical industry in drug safety. Currently I am a Medical Director for Wellpoint Corporation in which I have responsibility for medical leadership in Medicare Part D programs and products. This position involves the development of medical policies involving drugs, drug formularies, and assessing appropriate drugs for various senior patient populations.

This Supplemental Report addresses opinions and testimony of plaintiffs' experts that were expressed subsequent to my first report. In this report, I respond to the new opinions and analyses of Dr. Cheryl Blume and Keith Altman that are set forth in their Declarations. This supplemental report also addresses FDA's statistical review and evaluation of suicidality with antiepileptic drugs. I also offer opinions regarding Pfizer's conduct in the development, testing and labeling of Neurontin, which were not part of the general causation opinions in my first report. I hold the opinions expressed in this Supplemental Report to a reasonable degree of medical and scientific certainty, and these opinions are based on my education, training, experience, and my review of the relevant scientific and medical literature. I adopt and incorporate by reference my original general causation expert report. I have read and reviewed the supplemental expert reports of Dr. Sheila Weiss Smith and Dr. Robert Gibbons, and I adopt and incorporate by reference the contents of those reports. I reserve the right to review and rely upon subsequent literature and reports filed by other experts in this litigation.

A list of additional materials considered for this Supplemental Report is attached as Exhibit 1. My current CV is attached as Exhibit 2.

I practiced medicine as a specialist in internal medicine and rheumatology for 16 years. This experience extensively involved the selection of drug therapies for patients with chronic

unrelenting diseases and making observations of the safety and effectiveness of drug therapies in my patients. This clinical experience enabled me firsthand as a physician to appreciate the necessary observational components of “challenge dechallenge and rechallenge” phenomenon in patients receiving drug therapy with suspected adverse events and the limits to which such isolated phenomenon could be used to draw scientific inference about any causal relationships between an observed clinical phenomenon and an administered drug.

Over the past 20 years, I have accumulated substantial clinical, computational, pharmacovigilance and pharmacoepidemiology experience that includes individual patient care, the use of medical data to draw scientific inference and the representation and analysis of medical data from multiple data sources. All evidence that I have reviewed in this case neither suggests nor supports a casual relationship of Neurontin to suicide, suicidal behaviors, suicidal ideation and clinical states related to suicidality.

Pfizer’s procedures and methods in performing pre approval safety surveillance were sound and scientifically rigorous. Those efforts indicated no emergent risks with respect to Neurontin and suicide. Pfizer’s postmarketing pharmacovigilance methods, practices and procedures which incorporated postmarket adverse event data were sound and appropriate and met existing regulatory standards. Safety review meetings were conducted at reasonable intervals and incorporated topics that were driven by adverse event reports captured in the Pfizer adverse event report database and or literature. Pfizer was responsive to regulatory agencies when questions were presented to them regarding Neurontin safety issues. Pfizer incorporated methods and data sources requested by those agencies which included the FDA. Pfizer’s regulatory and safety practices resulted in appropriate Neurontin product labeling that accurately communicated the known risks of suicidality associated with Neurontin in its safety information. Pfizer’s labeling content was appropriately based on the best data available, which consisted of data from randomized placebo-controlled clinical trials and postmarketing experience for the drug. The FDA played an active role in reviewing and approving Pfizer’s procedures, conclusions, and language with respect to labeling. Following a comprehensive review of the Neurontin clinical trial and postmarketing data, additional or new Neurontin-specific suicidality warnings have never been requested or imposed by the FDA.

The FDA's meta-analysis of the clinical trial data of 11 antiepileptic drugs ("AEDs") provides no evidence that Neurontin itself is causally associated with suicidality and thus is not a basis for additional labeling, nor does it reflect adversely on the fact that Pfizer's pharmacovigilance efforts did not identify a potential risk of suicide with Neurontin since no scientific study or analysis has concluded such a risk exists. More importantly, the FDA's meta-analysis does not provide any support for plaintiffs' contention that Pfizer missed a signal for suicidality that would have warranted Neurontin-specific additional/different warnings for suicidality.

The FDA began to investigate the question of suicidality for AEDs in 2005. The FDA examined the prospective randomized placebo-controlled clinical trial data for 11 AEDs (carbamazepine, divalproex, felbamate, gabapentin, lamotrigine, levetiracetam, oxcarbazepine, pregabalin, tiagabine, topiramate, zonisamide). The FDA published an Alert in January of 2008 based on its preliminary results from its analysis. The FDA subsequently published the results of its analysis on May 23, 2008 in a Statistical Review and Evaluation, and the FDA's findings were discussed in detail at an Advisory Committee meeting held on July 10, 2008.

Because I spent considerable time examining data and applying the accepted scientific standards in interpreting data relevant to this action, I was familiar with Pfizer's analysis of its clinical trial and postmarketing adverse event data. I was concerned to learn of the FDA Alert regarding AEDs and suicidality. I emailed the then chief for the Center of Drug Evaluation and Research about the basis for the FDA's conclusions. In that communication, I asked about the relevance of spontaneous adverse event report data in reaching their conclusions. The FDA's response confirmed my conclusion that this type of data had no utility in drawing any inferences about a relationship of Neurontin to suicide or suicide behavior. At the Advisory Committee meeting regarding the FDA analysis of AEDs and suicidality, Dr. Russell Katz of the FDA confirmed the FDA's position regarding spontaneous adverse event reports:

*"...we had long ago decided that postmarketing data are not the right data to look at, or we don't believe that these sorts of things where there is a high background rate of suicidality so defined in these populations, I think that we have concluded that postmarketing data is uninterpretable, and that is why we went to placebo-controlled trials."* (FDA Transcript 2008, Dr. Katz. page 103)

On the other hand, the basis for the Citizens' Petition and the plaintiffs' assertions in this matter are based on spontaneous adverse event data sources that have been dismissed by the FDA as inadequate to scientifically evaluate whether Neurontin is associated with or causes suicide or suicide behavior. I concur with the FDA in the designation of spontaneous adverse event data as inadequate to address these questions. The FDA requested and analyzed this randomized placebo-controlled clinical trial data and never required a Neurontin-specific suicidality warning in the product labeling.

Contrary to plaintiffs' assertions in this matter, the FDA's meta-analysis does not provide any evidence to conclude that Neurontin itself is causally associated with suicidality. To draw such a conclusion based on the FDA's meta-analysis is scientifically unsound. The FDA's meta-analysis was not designed to test either the hypothesis that AEDs cause suicide, or the hypothesis that Neurontin causes suicide. This issue was addressed at the Advisory Committee meeting and Dr. Levenson of the FDA confirmed that the analysis applied to the entire data set of 11 AEDs:

Dr. Twyman: Let's assume that the effect is generalizable to the class of AEDs, but if you look at the compounds individually could one draw the conclusion individually that compounds have a risk. Or do you need to the entire data set of all AEDs put together in order to draw the conclusion that AEDs have a signal?

Dr. Levenson: I would say we need the entire data set in this case. July 10, 2008 Advisory Committee meeting transcript at p. 183 – 184.

Additionally, the FDA meta-analysis does not support plaintiffs' assertions that Pfizer missed a signal for suicidality, nor does it support plaintiffs' assertions that Pfizer should have performed a similar analysis on the Neurontin data. Further, the FDA's meta-analysis does not support plaintiffs' assertions that Pfizer should have placed a warning in the Neurontin label regarding suicidality. It is important to remember that the FDA, in its meta-analysis of AED prospective randomized placebo-controlled clinical trials collected data from 199 different clinical trials, with 43,892 patients, from 11 different AEDs, to show an association between AEDs and suicidality. Because of the well established limitations of meta-analytical approaches, one cannot draw a conclusion that a signal exists for any individual AED for suicidality based on the FDA meta-analysis. The findings of the Advisory Committee are consistent with my position. The Advisory Committee's findings certainly do not suggest that a signal with Neurontin exists, nor do they

suggest that Pfizer should have found a signal for Neurontin alone. In fact, the FDA's own data, presented in the Statistical Review and Evaluation, show that there was not a statistically significantly increased risk for suicidality with Neurontin.

Even though the spontaneous adverse event data is inadequate to address this question, when accepted standard analytic approaches to this data are nonetheless applied they indicate that no signal exists and, thus, provides no basis for the Citizens Petition or plaintiffs' assertions. I have also reviewed the analysis in the December of 2007 report of Dr. Sheila Weiss Smith and I agree with her conclusions that the Neurontin postmarket spontaneous adverse event data do not suggest a signal for suicidality.

Meta-analysis is a statistical method that combines data from several studies for the purpose of integrating the findings. By its inherent definition, meta-analysis invokes many issues and assumptions that limit its ability to support scientific inference; the FDA's statistical meta-analysis is not a substitute for a prospective randomized placebo-controlled clinical trial, and does not overcome the limitations inherent in meta-analytic approaches and cannot be used for the generation of scientific conclusions about causation. The limited utility of meta-analysis can be further degraded when components of the meta-analysis are inappropriately selected. The AEDs studied by the FDA in this meta-analysis are known to have different chemical properties, and the placebo-controlled clinical trials for these AEDs involved patient groups that were not homogeneous.

The meta-analytic approach used by the FDA cannot and has not added any more precision, accuracy, or rigor for establishing a relationship between Neurontin and suicide and suicide behavior beyond what has been established in randomized control trials. One cannot infer any causal relationship for Neurontin and suicidality from the FDA meta-analysis. This approach cannot replace, and is not a surrogate for, the precision, accuracy, or power of the prospective randomized control trial data. The limits of meta-analyses are well documented by the Gibbons report and prior testimony in this matter, as well as the epidemiological literature. Specifically, the FDA's meta-analysis of AED clinical trials suffered from a number of methodological flaws including: failure to properly assess trial heterogeneity, exclusion of trials that had zero events, misclassification of the various AEDs into non-mutually exclusive categories based on purported

pharmacologic mechanism and trial indications. The approach taken by the FDA in this meta-analysis may have served the need for the FDA to find a basis to issue a communication (which specifically stated that it did not conclude a causal relationship of any agent to suicide) as a matter of regulatory procedure to clinicians, but scientifically is insufficient to address the question of a causal relationship of suicide or suicide behavior to Neurontin.

Plaintiffs incorrectly claim that the FDA meta-analysis helps to establish a causal relationship between Neurontin and suicidality. The FDA meta-analysis was based on AED randomized placebo-controlled clinical trials designed and conducted differently, in different selected study populations, and involving drugs with different chemical and pharmacologic properties. Meta-analysis summarizing the results of 11 different AEDs cannot provide meaningful scientific insight on any one of the 11 AEDs. It is possible that if one combines individual randomized clinical trial studies of the same drug it is possible to address a scientific question regarding a potential safety concern regarding that drug. This was in fact the approach that drove the Pfizer analysis submitted to the FDA that combined all randomized clinical trial studies for Neurontin and combined data to improve power and precision (Evertz 2006). The finding of the Evertz 2006 submission indicated no excess risk with respect to suicide or suicidal behavior in Neurontin studies.

The findings of the FDA meta-analysis and the Advisory Committee regarding the 11 AEDs do not support any hypothesis or opinion that Neurontin causes suicidality. Despite Dr. Russell Katz's statement at the Advisory Committee hearing that he was "comfortable with the 'c word'," the actions of the Advisory Committee show that the committee felt it necessary to distinguish causality from a "signal." The original question the FDA posed to the Advisory Committee was whether the committee agreed "with the Agency's overall finding of an increase in suicidality for the 11 AEDs analyzed." However, after much discussion, the question was substantially changed to "Is there a signal?" In addition, the Advisory Committee voted to not include a Black Box warning for suicidality; indeed, no decisions were made as to any specific warnings regarding suicidality for any of the AEDs considered, much less for Neurontin alone. These actions and interpretations of the FDA meta-analysis by the Advisory Committee contradict any assertion that the meta-analysis provides sufficient scientific rigor to support a conclusion of a causal association between Neurontin and suicidality.

It is important to note that the FDA and the Advisory Committee, in their deliberations, did not conduct a consideration of causality as set forth in epidemiology texts or the FDA guidance documents. Nor did the FDA employ methods set forth in the reports or Declarations of Dr. Blume or Mr. Altman. The generalizability of the findings of the FDA's meta-analysis are extremely limited because of the meta-analytic approach and the influence of confounding by disease indication, i.e. confounding by the fact that one cannot separate out the risk of suicide and suicidality that is inherent in the underlying diseases themselves. The meta-analysis may merely set forth an hypothesis of a potential signal or association between 11 AEDs and suicidality to provide a basis for issuing a medical provider communication. The FDA analysis does not set forth the hypothesis of a potential signal or association between Neurontin and suicidality; in fact, the FDA found no statistically significant association between Neurontin and suicidality (based on odds ratio and risk difference calculations) based on the randomized clinical trial data for Neurontin. Thus, it is inaccurate and incorrect for plaintiffs' experts to suggest that the FDA's meta-analysis supports a causal role of Neurontin for suicidality.

The FDA in their meta-analytic approach used a similar technique that led to a black box warning for antidepressant drugs in pediatric and adolescent patients. Since the issuance of that warning in 2003 the Centers for Disease Control have tracked a steady rise in the rates of teen suicide. This is a trend that reversed a steady downward trend to that point in time of teen suicide. A study in the September 4, 2008 Journal of the American Medical Association shows that this trend correlates with a declining use of antidepressant drugs in adolescents as a result of the FDA warnings. If the meta-analyses used by the FDA were adequate to prove that antidepressants cause suicide, then a continuing downward trend or more dramatic drop in teen suicide rates should have been observed with the decline in use of antidepressants; a result that did not occur following the FDA's meta-analysis and the resulting black box warning.

Again, while the meta-analysis method may be sufficient to prompt a precautionary communication by the FDA, it does not prove causality and may lead to unintended public health consequences. The Advisory Committee transcript indicates that certain members were concerned about over-warning.

The assertions of Cheryl Blume and Keith Altman that Neurontin causes, or is capable of causing, suicidality are not supported by appropriate methods or the evidence. Blume and Altman's assertions that Neurontin causes suicidality are based on anecdotal evidence, which Webster's Dictionary defines as "based on unscientific evidence". Blume considers isolated spontaneous adverse event reports that contain clinical information as her "anecdotal" evidence of a relationship between Neurontin and suicide adverse events. In her Declaration, she states that this "anecdotal" evidence "suggests" such a relationship. Blume is not a physician and has no medical training and has no ability to evaluate the clinical content and concepts within these anecdotes.

Data from uncontrolled spontaneous adverse event reports cannot provide sufficient scientific evidence to evaluate the hypothesis of a relationship between Neurontin and suicide adverse events. Analyses of isolated uncontrolled spontaneous adverse event reports cannot be used to support Blume's assertion of a relationship between Neurontin use and suicidality, since these reports are not compared to reports of patients who successfully use Neurontin with no or diminished risk of adverse events, nor are they compared to the adverse event experience of the same types of patients not taking Neurontin. Studies that incorporate observations of comparator groups provide a sound basis for scientific inferences on the potential relationship between medicines and adverse events, and Blume fails to make these comparisons and conducted no such study.

Blume incorrectly states that Pfizer was negligent in not aggregating suicide or suicidal behavior adverse events with types of adverse events that have no relation to suicide or suicide behavior. To aggregate adverse events that are not suicide, nor that bear any clinical or pathophysiological relationship to suicide or suicide behavior, is inappropriate methodologically not only because it is akin to adding apples and oranges, but it also carelessly dilutes and undermines the precision for which adverse event coding systems were designed to provide. Such methodological errors, in attempt to create a safety concern that does not exist, threatens the health of patients for whom Neurontin has safely provided therapeutic benefits. The aggregation approaches used by Pfizer were sound and were accepted practice as defined by standards of pharmacovigilance practice, and correctly evaluated adverse events coded with suicide and suicide related terms with appropriate sensitivity and specificity with regard to safety signal detection.

Blume states that she relies on the causality assessments made by clinical trial investigators for adverse events that occurred during the trials. It is important to note, however, that Blume confuses the meaning of causality assessment in the context of conducting clinical trials. Although it is standard practice in the evaluation of individual clinical trial adverse events for the investigator to make a “causality assessment” in adverse event reports, and rank the probability that the drug may have caused or contributed to the reported adverse event in the study subject, this required statement does not scientifically establish causation between the drug and the observed event in that study subject. Isolated, individual causality statements by individual investigators are their opinions and are subject to definitions set forth in the study protocols and biases, including the bias that the statements err on the side of attributing causality. Such individual observations are required to be reported for regulatory purposes. They are not, in themselves, sufficient to scientifically establish causality. Furthermore, they do not surpass the strength and power of the entire clinical trial method, which aggregates and statistically compares all reported adverse events regardless of individual investigator assessment. These Individual observations can provide a pharmacovigilance approach to suggest a signal or hypothesis, but are insufficient to confirm or determine causation.

Blume asserts in her Declaration that Pfizer should have, as early as 1994, used a protocol similar to that set forth in the “Gabapentin Capture Aid.” Blume Declaration at ¶ 38. Blume mischaracterizes this document, as the purpose of the Gabapentin Capture Aid was to “systematically collect and assemble all available information...involving adverse events of special interest,” to provide “additional lines of inquiry designed to gather supplementary data,” and to “help to ensure accurate and timely characterization of the reported adverse events including the relative contributions of potential etiological factors to the occurrence of the selected events.” NREXE2091004141 at p. 1. The Gabapentin Capture Aid served as an additional tool to help gather data on suicidality, but Pfizer performed diligent pharmacovigilance prior well before the implementation of the Gabapentin Capture Aid. The Gabapentin Capture Aid helped to gather data, but, contrary to Blume’s assertions, it did not set forth a protocol for analyzing data and/or interpreting data; this document was not designed to replace clinical and medical judgment in interpreting the data collected.

Blume asserts that setting the threshold for of detection of events occurring at a rate of 1% or greater of the total number of events would preclude capture of events such as suicide attempt, which reached the 0.24% level, and she incorrectly asserts that the Gabapentin Capture Aid indicated groupings of events that should have been analyzed instead. See Blume Declaration at ¶ 40. Blume ignores the fact that the Gabapentin Capture Aid does not suggest grouping of adverse event terms, but rather lists terms that trigger the use of the Aid. Moreover, Pfizer used appropriate medical judgment and approaches to identify potential safety concerns from adverse event reports that occurred above and below the threshold of 1%, based on the seriousness of the events. Blume, not being a clinician, cannot understand the clinical and medical judgments used by medical professionals at Pfizer in assessing adverse events that occurred in frequencies above and below the threshold of 1%.

Pfizer's Core Working Group appropriately reviewed events coded with preferred terms of suicide or suicide attempt. Decisions not to include those terms in the Neurontin warnings were based on the absence of sufficient evidence. Pacella deposition at 208:25 – 209:11. In 2004, Pfizer comprehensively evaluated whether the available Neurontin data demonstrated an increased risk for suicide or suicidal behavior and again came to the appropriate conclusion that no such risk existed. Blume never performed any clinical or medical analysis beyond merely tabulating raw counts or plotting percentages of adverse events or groupings of adverse events. The inability of Blume to perform any clinical or medical review of adverse events invalidates her opinions based on those counts of adverse events.

Blume states that convincing dechallenge/rechallenge reports exist and that they provide convincing evidence of a relationship of Neurontin to suicide and suicide risk. I have examined the reports identified by Blume as dechallenge/rechallenge phenomenon and none of these meet the criteria of a valid dechallenge/rechallenge adverse event. The phenomenon measured in all these reports is subjective (dependent upon patient reporting to the physician); these events are not time discrete and cannot be objectively and verifiably consistently measured. Because of their subtle nature, these events could have occurred or could be occurring before patients received Neurontin. Dechallenge/rechallenge events in psychiatric patients can be highly influenced by the mere fact of a drug being discontinued or reintroduced, especially if there is some belief that the drug may be related to the symptom. Such bias renders dechallenge/rechallenge events in this, or any, population unusable for the purposes of

assessing causality. In addition, the patterns cited by Blume in dechallenge/rechallenge cases with so-called “re-immergence” of suicidality are not consistent with the known pharmacokinetic profiles of Neurontin.

Nowhere in her most recent Declaration or in previous testimony does Blume use or attempt to use the concept of incidence rates as a measure of risk or relative risk of suicidality, a type of adverse event that is intertwined in the clinical spectrum and natural history of seizure, depression, bipolar disorders, anxiety and pain patient populations due to the disease process itself, even when such data has been made available. Such an analytic approach is core to methods used to quantitatively assess the probability of an event occurring and the relative probability of the occurrence of an event in the presence of an exposure or factor relative to the probability of the event occurring in the absence of the exposure. This approach is the strongest type of evidence, when available, in hypothesizing the existence of a possible causal association (i.e. a gold standard: Reference Manual on Scientific Evidence). In fact, the FDA suggests that “to provide further context for incidence rates or reporting rates, it is helpful to have an estimate of the background rate of the occurrence for the event being evaluated in the general population or, ideally, in a subpopulation with characteristics similar to that of the exposed population.” March 2005 Guidance Document on Good Pharmacovigilance Practices. No where in Blume’s reports or analyses were data used that enabled calculation of rates or relative rates of suicide, or suicide behavior (measure of risks and relative risk).

Overall, Blume highlights raw numbers of adverse event reports, but she does not calculate rates which provide a measure of risk and are necessary to identify excess risk. Nor does she compare rates among comparator groups. She does not compare the rate of suicide in Neurontin patients with those of patients receiving placebo. She identifies adverse event reports of patients taking Neurontin, but does not identify, recognize, or consider any potential reports or studies of patients taking Neurontin successfully without adverse events. She relies on data sources that do not allow for the reporting or capturing of data that would represent the absence of suicide or suicide-related adverse events in patients using Neurontin. When such data exists, her methods ignore it.

Blume states that the FDA, in the Code of Federal Regulations (Chapter 21 Code of Federal Regulations) in Section 201.57(e), provides information on the relative role or value of epidemiological evidence in establishing scientific associations. Blume Declaration at ¶19. Nowhere in Chapter 21 of the Code of Federal Regulations is there scientific discourse or discussion to regulate, govern, or determine what constitutes sufficient evidence to draw scientific inference, nor is that the intent of this regulation. Blume misquotes and misrepresents the content of the Code of Federal Regulations Chapter 21. First, there is no paragraph or section (e) in Section 201.57 Chapter 21 of the Code of Federal Regulations. Second, nothing in that document speaks to relative merits of different types of evidence for drawing scientific inference. The entire Section 201.57 relates to product labeling, and does not address the relative merits of scientific evidence. The only content within that section to which Blume makes reference and that relates to the topic of "Black Box" is as follows:

(1)*Boxed warning*. Certain contraindications or serious warnings, particularly those that may lead to death or serious injury, may be required by the FDA to be presented in a box. The boxed warning ordinarily must be based on clinical data, but serious animal toxicity may also be the basis of a boxed warning in the absence of clinical data. The box must contain, in uppercase letters, a heading inside the box that includes the word "WARNING" and conveys the general focus of the information in the box. The box must briefly explain the risk and refer to more detailed information in the "Contraindications" or "Warnings and Precautions" section, accompanied by the identifying number for the section or subsection containing the detailed information.

The information in this paragraph directly contradicts Blume assertion. This paragraph does not state, as Blume suggests, "that epidemiological evidence is not indispensable" but rather that clinical trial data supersedes animal data and must be the basis for black box warning when it exists. The section in Chapter 21 of the Code of Federal Regulations that Blume attempts to represent states that animal data may have relevance only when clinical trial data does not exist. Animal data in the context of the abundant clinical trial data and almost 15 years of extensive clinical use in patients shows no relation of Neurontin to suicidality. Blume's interpretation of the content of this regulation is incorrect.

Blume's assertion that "the absence of evidence is not evidence of absence" contributes no evidence in support of the plaintiffs' assertions. Blume states that there exists no epidemiological evidence that an association does not exist between Neurontin and suicide or suicide behavior. Epidemiological evidence can in fact support the null hypothesis that no association exists between an exposure and an event for a given population and can result in sound methodological rejection of the alternative hypothesis, that an association does exist for the population studied. The null hypothesis that no association exists between Neurontin use and suicide or suicide behavior has been supported by the randomized control clinical trial data in the Neurontin clinical development program.

The only reliable evidence that does exist relevant to the question of Neurontin association with suicide or suicidal behavior are the clinical trials, which have correctly, validly and consistently demonstrated the absence of an association of suicide or suicide behavior in association with Neurontin. Additionally, Blume completely ignores the fact that the FDA's meta-analysis of the prospective randomized clinical trials of 11 AEDs shows that there is no statistically significant increased odds ratio or risk difference of suicidality for Neurontin.

Pfizer, in its pharmacovigilance practices and in its safety analyses requested by regulatory agencies, collected and analyzed data from multiple sources including spontaneous adverse event reports. These include adverse events in individual controlled clinical trials, and, for purposes of increasing statistical power, analyzed data from all clinical trials in combination. Pfizer also included evaluation of case series and individual adverse event reports. Pfizer evaluated these reports individually and collectively with qualified medical, drug safety, and analytic experts.

At the aggregate level, Pfizer appropriately and systematically analyzed and queried its database of adverse event reports for patterns and set appropriate thresholds given the limitations and constraints of spontaneous adverse event report data. The results of those queries were presented at Core Labeling meetings with clinical experts and analytic experts who systematically identified signals and applied sound medical and quantitative expertise to interpreting those signals. (Current Challenges in Pharmacovigilance: Pragmatic Approaches: Report of CIOMS Working Group V Geneva 2001, CIOMS V).

Pfizer's pharmacovigilance practices met accepted standards for postmarket safety surveillance during the relevant time period. Pfizer identified and collected information continuously and regularly over time on spontaneously reported adverse events according to accepted regulatory and scientific standards. As such, the labeling for Neurontin accurately reflects and appropriately informs prescribing physicians of the relevant information pertaining to suicidality. Plaintiffs incorrectly assert that Pfizer missed a signal for suicidality that would have warranted different or additional warnings or precautions.

11/00/08

Date



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